Potential Prospective Application of Zr-Based Bulk Metallic Glasses in Dental Implant

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Zr-based bulk metallic glasses (BMGs) are being studied widely in recent years due to their unique mechanical properties. In this paper, we will present the progress in the studies of corrosion resistance behavior and biomedical potential of the Zr-based BMGs, especially the in vitro and in vivo evaluation of their biocompatibility. Owing to their high resistance to corrosion in a physiological environment and the excellent biocompatibility that give them a passive, stable oxide film, Zr-based BMGs are considered the material of choice for intraosseous use. The aim of this paper is to give an overview of the available literature on the Zr-based BMGs and present a promising prospect for the application of oral implant.


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Keywords: bulk metallic glasses (BMGs), dental material, biocompatibility, corrosion resistance, bioactive surface modification

1. Introduction

Tooth loss is very common and often happens in aging population and mechanical injuries, therefore, orthopedic prostheses or dental implants are necessary. The use of dental implants to support replacement of missing teeth has a long and multilayered history.1,2) Despite the considerable clinical success of present implant materials, multiple factors including stress shielding, particle disease, fatigue failures, and corrosion, have led to an undesirable impact on their practical performances.3,4) Ti and Ti alloys are now mainly used for implant applications.5-8) However, there are some studies that show Ti and its alloys might be an allergen.9-11) Moreover, the elastic modulus of biomedical Ti and its alloys are usually above 100 GPa, which is much higher than the natural bone. The mismatch in the elastic modulus will produce stress-shielding effect, which can lead to bone resorption for long-term use. A new biomedical alloy, Bulk Metallic glass, is desirable, which has low elastic moduli to avoid stress shielding, high wear resistance to reduce wear debris, high corrosion and fatigue resistance to resist the harsh in vivo environment.12) Moreover, such implant device may be protected from cyclic loading during masticating. Therefore it is critical to understand its fatigue behaviors in human oral cavity, and to find a new kind of biomaterial which is not only well mechanical, but also possesses good biocompatibility.

Metallic glasses were discovered in 1960, when Duwez et al.13) purified an Au-Si alloy by quenching rapidly from the molten state. Since then, due to a flood of research of the alloy, the characteristics of many other amorphous alloys have been investigated from various viewpoints owing to their unique properties. Amorphous alloys show higher tensile strength than crystalline alloys in the same chemical composition, with lower Young’s modulus when the tensile strength is same; the corrosion resistance of amorphous alloys is also superior to that of crystalline alloys with same chemical composition.14) Further, in the later 1980s, a class of multicomponent amorphous alloys were discovered, which had much lower critical cooling rates and permitted amorphous metallic materials to be produced in bulk consisting mainly of ordinary metallic elements with minimal dimensions of 1 mm.

Recently, a growing attention in BMGs has paid in particular to the Zr-based BMGs due to their good mechanical and material properties. Table 1 shows some material and mechanical properties of some implant alloys.15,16) Compared with other alloys, Zr-based BMG shows superior yield strength, elastic strain, Vickers hardness; it also owns relatively low plastic strain, and toughness. The Young’s modulus of Zr-based BMG is much closer to the natural bone, which will help preventing the stress-shielding effect. Some researchers also found its high corrosion resistance and good formability in the super cooled liquid region.17-21) Since the fatigue behavior is an important characteristic of structural materials, Morrison et al.22) reviewed the fatigue studies of Zr-based BMGs and their composites, and found that they have an excellent loading fatigue, not only plain fatigue in air but also cyclic fatigue in pseudo-body fluid.

Therefore, Zr-based BMGs are desirable candidate materials for biomedical application, with the combination of favorable mechanical properties, attractive corrosion resistance and biocompatibility.

In this paper, we will present the progress in the studies of corrosion resistance behavior and biomedical potential of the Zr-based BMGs, especially in vitro and in vivo evaluation of their biocompatibility. And give an overview of the available literature on the Zr-based BMGs and present a promising prospect for the application of oral implant materials.

2. Properties

2.1 Corrosion behavior

Metal alloys implant is being corroded in human bodies, because body fluid contains electrolyte and in most cases is subject to cyclic loading. Types of the corrosion are pitting, fretting and fatigue. One of the fundamental aspects of biocompatibility that should be carefully assessed is the electrochemical interaction that inevitably leads to the release

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of metal ions into the vicinity tissue. Therefore, the corrosion behaviors of the Zr-based BMGs, a promising candidate of implant materials, should be evaluated in a physiologically relevant environment.

Gebert et al.\textsuperscript{23} firstly investigated the electrochemical behavior of Zr-based bulk metallic glasses. Hiromoto et al.\textsuperscript{24-26} explored the effects of surface finishing, chloride-ion concentration, pH value and dissolved oxygen pressure on the electrochemical polarization of Zr\textsubscript{65}Cu\textsubscript{17.5}Ni\textsubscript{10}Al\textsubscript{7.5} BMG in the phosphate buffered saline (PBS) solution. The result indicated that the BMG had similar polarization behavior to pure Ti, and showed pitting corrosion resistance in a wide range of pH value, chloride-ion concentration, and dissolved oxygen pressure. Furthermore, Hiromoto and Hanawa\textsuperscript{27} performed a further study on re-passivation of the alloy in a Hank's balanced solution, and found that its re-passivation current density was lower than the ingredients crystal alloy. Murayama et al.\textsuperscript{28,29} conducted the stress-life curves through uniaxial-fatigue tests with plate specimens of the Zr-based BMG (Ni\textsubscript{7.6}Cu\textsubscript{12.3}Al\textsubscript{3.5}Zr\textsubscript{76.6}) in PBS and in air respectively. The result showed there was no difference between the stress-life curves of plain fatigue in air and in PBS. Gebert et al.\textsuperscript{30} confirmed that the corrosion occurred in the structure defect of the sample. In both environments, its fretting fatigue behavior demonstrated little difference in the friction coefficient and in the film-forming compositions fretted surface.\textsuperscript{29} However it was found that there were different elements of the oxide films on their surfaces, indicating that the fretting fatigue strength was related to the difference of the elements of the oxide films.\textsuperscript{31}

Morrison et al.\textsuperscript{10} conducted the cyclic anodic polarization of the Zr\textsubscript{55}Cu\textsubscript{17.5}Ni\textsubscript{14.6}Al\textsubscript{10}Ti\textsubscript{5} BMG (Vit 105) in PBS electrolyte with physiologically relevant oxygen content at 37°C. The result showed there was a more considerable corrosion penetration rate (CPR) than the CoCrMo and the TiAl\textsubscript{6}V\textsubscript{4} alloys, and lower CPR than the 316L stainless steel. As previously discussed, the Zr-based BMGs’ counterface wear resistance and bone cement abrasion resistance were better than the conventional cast CoCrMo\textsubscript{6}.\textsuperscript{32} For example, the Zr\textsubscript{60}Cu\textsubscript{22.5}Pds\textsubscript{3}Al\textsubscript{7.5}Nb\textsubscript{5} BMG alloy, a kind of the Zr-based BMGs, showed an excellent corrosion resistance and a good biocompatibility in the artificial body fluid.\textsuperscript{33} Liu et al.\textsuperscript{34} examined the corrosion behavior of some Zr-based BMGs in three different environments, namely PBS, artificial saliva solution (ASS) and artificial blood plasma solution (ABP).

Table 1 Mechanical and material properties of some alloys for implant.\textsuperscript{15,16} $E$ is the Young’s modulus (GPa), $Y_s$ is the yield strength (MPa), $FL$ is the fatigue limit at 10$^7$ cycles (MPa), $ES$ is the elastic strain (%), $PS$ is the plastic strain (%), $D$ is the density (g/cm$^3$), $H$ is Vickers hardness ($HV$) and $T$ means toughness (MPa).

<table>
<thead>
<tr>
<th>Alloys</th>
<th>$E$</th>
<th>$Y_s$</th>
<th>$FL$</th>
<th>$ES$</th>
<th>$PS$</th>
<th>$D$</th>
<th>$HV$</th>
<th>$T$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoCr alloys</td>
<td>210–255</td>
<td>450–1030</td>
<td>207–970</td>
<td>0.18</td>
<td>8–28</td>
<td>8.5</td>
<td>345–590</td>
<td>—</td>
</tr>
<tr>
<td>Ti6Al4V</td>
<td>124</td>
<td>830</td>
<td>598–816</td>
<td>0.67</td>
<td>10</td>
<td>4.4</td>
<td>320</td>
<td>65–92</td>
</tr>
<tr>
<td>Cortical bone</td>
<td>3–50</td>
<td>80</td>
<td>20–60</td>
<td>20–60</td>
<td>2</td>
<td>1.9</td>
<td>63–75</td>
<td>3.2–8</td>
</tr>
<tr>
<td>Zr-Based BMG</td>
<td>90</td>
<td>1700</td>
<td>—</td>
<td>2–2.2</td>
<td>0</td>
<td>5.9</td>
<td>590</td>
<td>55–60</td>
</tr>
<tr>
<td>(ZrCu\textsubscript{17.5}Ni\textsubscript{14.6}Ti\textsubscript{5}Al\textsubscript{10})</td>
<td>90</td>
<td>1900</td>
<td>910</td>
<td>2–2.2</td>
<td>&lt;1</td>
<td>5.9</td>
<td>590</td>
<td>55–60</td>
</tr>
</tbody>
</table>

The results showed all BMGs exhibited superior corrosion resistance. Huang et al.\textsuperscript{35} reported the friction and wear behavior of the Zr-based BMG under sliding in distilled water, dry air and PBS respectively. Moreover, the results showed the environments had little effects on crack-initiation region and the fatigue life of the BMG.\textsuperscript{36}

Nowadays the mechanism of the corrosion is still not clearly understood. Usually it is thought that the corrosion behavior of the BMGs is originated in the deformed, as-cast and relaxed. Jiang et al.\textsuperscript{37} investigated that the pitting corrosion was enhanced due to the decrease in free volume factors by reducing pit propagation. This phenomenon suggested that we should consider the change in the formation of clusters and the chemical order caused by the relaxation annealing. Deformation-induced residual stress, external electrolyte and surface shear offset effect can all lead to preferential pitting near the shear band, therefore a lot of people involved in the research on this aspect. Gebert et al.\textsuperscript{38} and Wang et al.\textsuperscript{39} determined to identify the causes of preferential pitting corrosion in the vicinity shear bands, and found that local structural and chemical changes played an important role in pitting initiation due to the presence of dislocation, formation, weak or sensitive point near shear bands. Later, Nie et al.\textsuperscript{39} confirmed that the pitting initiation occurred in the shear bands under certain condition, which was mainly attributed to the structural changes in the shear bands. Subsequently, Wang et al.\textsuperscript{40} thought that the shear offsets resulted in pitting initiation rather than the shear bands themselves, which meant that the pitting corrosion had little relation to the structural change. Moreover, it was found that the heterogeneous structures reduced corrosion resistance by comparing three different BMGs.\textsuperscript{41} Monfared et al.\textsuperscript{42} showed that all BMGs were small by contacting angle measurements, which meant that they were hydrophilic and the cell adhesion might be enhanced in the biomedical applications.

Furthermore, the addition of trace elements had also an effect on the resistance improvement. For example, Ti element addition to the ZrCuAlFe BMGs exhibited a significant pitting corrosion resistance improvement. Due to the addition of a small amount of Ag to the Zr-based BMGs, the formation ability and the mechanical properties of the BMGs were greatly improved, which meant that the application potential of the material was increased in the biomedical field.\textsuperscript{43–45} and Ag also enhanced the corrosion...
resistant of the BMGs.\textsuperscript{46,47} Furthermore, the effect of adding Nb to the BMGs was also very significant. This addition would lead to a lack of sensitivity to chloride ion.\textsuperscript{38,49} Another two available additions, namely Pb and Y, increased corrosion resistance of the BMGs.\textsuperscript{50–52}

Generally, amorphous alloys have gained the reputation of excellent corrosion resistant materials which is attributed to their chemically and structurally homogeneous nature, that is, providing a lack of local electrochemically active sites. Moreover, adding some trace elements can improve the alloys’ corrosion resistance, which will enhance the performance of the alloys further by adding corresponding elements.

2.2 Biocompatibility

Evaluation of biological safety is an indispensable aspect of biomedical materials application, roughly divided into three steps, namely \textit{in vitro} test, animal test \textit{in vivo} trial and animal test in clinical trial. \textit{In vitro} test is the first crucial step, and generally detecting cytotoxicity is a simple but effective method in this step.\textsuperscript{53} Horton and Parsell\textsuperscript{15} carried out a series of tests on the biocompatibility of the BAM-11 (ZrAl\textsubscript{10}Ti\textsubscript{3}Cu\textsubscript{17.9}Ni\textsubscript{14.6}) by evaluating cellular viability on the BMG surface. It was found that BAM-11 showed as good biocompatibility as Ti and polyethylene. Löfler \textit{et al.}\textsuperscript{54} tested the Ni-free Zr-based BMG (Zr\textsubscript{55}Cu\textsubscript{22}Fe\textsubscript{9}Al\textsubscript{12}), and the animal cell culture test showed that the mouse viability and fibroblast-cells metabolism on the alloy treated by nitric acid was much closed to polyethylene. Later, Liu \textit{et al.}\textsuperscript{55} performed cell toxicity test of Ni-free Zr-based BMGs, and also confirmed good biocompatibility. Since cell adhesion test and protein adhesion test were two parts of the \textit{in vitro} biocompatibility tests, Huang \textit{et al.}\textsuperscript{56} carried out biocompatibility assays using human cells. It showed the level of protein adhesion was high, and cell adhesion and proliferation was good, which was far more accurate for medical material testing of Ni-free Zr-based BMGs. Furthermore, protein adhesion and cell adhesion protein test of Ni-free Zr-based BMGs also showed good biocompatibility.\textsuperscript{57,58}

Because hemolysis test was a part of blood compatibility, hematological compatibility and cellular responses of the BMGs were investigated. The round shape platelets with no pseudopodia spreading on the surface of alloys implied that the Ni-free Zr-based BMGs had good anti-thrombogenic properties in \textit{in vivo} environment. Furthermore, their low hemolysis rates suggested that the Ni-free Zr-based BMGs had no destructive effect on erythrocyte.\textsuperscript{59}

Previous studies mostly used fibroblasts to measure its cytotoxicity, and evaluate the interaction of the implant with bone by osteocyte response. Tissue rejection reaction is usually one of the main causes of implant failure, and the level of macrophage is a good estimate for the degree of tissue inflammation. So macrophage responses to (Zr\textsubscript{55}Al\textsubscript{10–15}Ni\textsubscript{3}Cu\textsubscript{30}Y\textsubscript{1}) (atomic percent) BMGs were examined. The result revealed a low level of macrophage activation. The level of proinflammatory cytokine, TNF-a, secretion from macrophages is not high.\textsuperscript{60}

Implantation is conducted in the animal test, which belongs to the pre-clinical tests of biocompatible materials. The evaluation of the histocompatibility of the BMGs was conducted by implanting BMG samples into white rabbits subcutaneous, and it showed that the BMG implants performed as well as the Ti alloy.\textsuperscript{61} Imai and Hiromoto\textsuperscript{62} used intramedullary nails in rat femora to make \textit{in vivo} assessment of the Zr\textsubscript{65}Al\textsubscript{15}Ni\textsubscript{10}Cu\textsubscript{15} BMGs. Compared with TiAl\textsubscript{6}V\textsubscript{4} alloy and 316L stainless steel, it showed lower levels of Cu and Ni in the blood and the surrounding soft tissue, and the intramedullary nails made of Zr-based BMG had no difference in promoting osteotomy healing time. These results fully demonstrated that the application of Zr based amorphous alloy in the biomedical field is promising.

2.3 Surface modification

Like other biometals, bioinert is also the Zr-based BMGs’ nature. To reach a tight chemical bonding with bone tissues as implant materials, the surface activation layer must be formed. Briefly, surface modifications are needed to make metal implants bioactive before they are applied in clinic.

Gerbet \textit{et al.}\textsuperscript{63} effectively improved the plasticity of BMGs through applying pre-deformation treatments by shot-peening. Surface modification of Ti alloy could selectively apply to the Zr-based BMGs. The treatment BMGs could show a good activity through microarc oxidation technology. Liu \textit{et al.}\textsuperscript{64,65} investigated the bioactivity of the MAO-treated samples which were immersed into simulated body fluid, and found that a bone-like apatite layer was successfully deposited on the surface of the Ni-free Zr\textsubscript{60.5}Cu\textsubscript{19.5}Fe\textsubscript{5}Al\textsubscript{9.5}Ti\textsubscript{5.5}. Through performing bioactive Ca titanate coatings on a Zr-based bulk metallic glass by laser cladding, the CaTiO\textsubscript{3} can spontaneously form the apatite on its surface when soaked in simulated body fluid to make the Zr-based BMGs surface bioactive.\textsuperscript{66} Li \textit{et al.}\textsuperscript{67} researched the Zr-based BMGs through sand blasting modification, and observed that osteoblasts responded to alloy modification and the increased wettability of surfaces led to higher cell attachment, cell proliferation, and differentiation properties compared with those of osteoblast MG63 cells. Ar and Ca ion implantation also increased corrosion resistant of the BMGs.\textsuperscript{68} Moreover, nitrogen plasma immersion ion implantation could enhance the bio-corrosion resistance of Ni-free ZrCuFeAl bulk metallic glass.\textsuperscript{69} Bioactivity is of great importance for biomaterials. Surface modifications, like MAO-treated, sand blasting modification, ion implantation and coating, are very common methods to improve surface-related properties, including wear and corrosion resistance.

3. Discussion

Inoue\textsuperscript{70} showed the design of BMGs should follow three empirical component rules: (1) Multicomponent consisting of more than three elements; (2) Significantly different atomic size mismatches exceeding 12\% among the main three constituent elements; (3) Negative heats of mixing among their main elements. There are still many works to be done in the future. Progress in designing novel BMGs to resolve aforementioned issues will definitely promote their applications as biomaterials in some field such as dental implant, artificial joint and femoral head support. Although there also are some intrinsic flaws which restrict the BMG’s widespread applications, such as lack of ductility which makes BMGs prone to catastrophic failure in load-bearing conditions, high
cooling rate which limits the glassy alloys geometry to thin sheets and lines. However, besides the good mechanical properties, one of the biggest advantages of the BMGs is that the material could form protective films both on the strong acid and alkali solution, and the passivation membrane can effectively reduce the rate of corrosion. The biomedical potential materials should not only show good mechanical properties, but also good biocompatibility on the application of BMGs in the biomedical field.\(^{(3)}\) Relative to the potential need for large-scale clinical practical application, Zr-based BMGs research as biomaterials is still in its infancy.

The minor addition technique is also playing an important and effective role in glass formation, improvement of thermal stability and the properties of BMGs. The research trend now is from Ni-containing BMGs to Ni-free BMGs, and the investigation included the forming ability, the mechanical and electrochemical behaviors, and the biocompatibility. The alloy composition as well as the purities is crucial for the glass formation. Although the Ni-containing BMGs have good mechanical properties, the Ni element is allergic and probably carcinogenic for the human body;\(^{(72)}\) therefore a lot of Ni-free BMGs are having been developed.\(^{(73)}\)

Talking about the effect of Cu, there are different ideas. On one hand, Cu could improve the plasticity of the alloys and show bacteriostatic action;\(^{(74)}\) on the other hand, when large quantities of heavy metals reside in the human body, the damage caused by the heavy metal ion of Cu is acute burden on the body’s organ.\(^{(75)}\) The addition of some element such as Ag, Ni, the formation ability and the mechanical properties of the BMGs may be greatly improved, however the amount and proportion must be accurately controlled.

Therefore, the future research should be done in the following aspects:

1. New design methods. Overcome brittle failure in tension BMG and observe corrosion fatigue by fatigue test in different physiological fluids;

2. More biocompatibility experiments. Explain the case of corrosion resistance on the bearing load. The research should not only be done in the test cell toxicity, but also carried out on bone implant test and pre-clinical tests.

3. Animal tests. Evaluate the biocompatibility of BMGs in both the in vitro biocompatibility test and in vivo animal test;

4. Addition and amount control of some trace elements.

Not only improve the BMGs’ corrosion resistance performance, surface modification and surface activity, but also have no or little influence on users.

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